REMARKS

Claims 33-36, 38-39, and 41-64 are all the claims pending in the application. Claims 38, 39, 43-52, and 57-58 are withdrawn, and claims 1-32, 37, and 40 have been canceled. Claims 33, 35, 36, 43, 45, 47, 55-56, and 61 have been amended. Support for the claim amendments can be found throughout the specification and originally filed claims.

Claim 35 has been amended to recite "wherein the region encodes a protease digestion site in the same reading frame as (a)" as suggested by the Examiner in response to a §112, second paragraph rejection.

Claim 36 has been amended to clarify the claim language.

Claims 43, 45, 47 originally depend from cancelled claim 37 and have been amended to depend from 33 instead.

Claim 55 has been amended to recite "[a]n isolated host cell" as suggested by the Examiner in response to a §112, first paragraph rejection.

Claim 56 has been amended to correct a typographical error.

Claim 61 has been amended to recite "the 5' terminus of a coding region of the expression vector that encodes the N-terminus of the fused protein," instead of "a 5' terminus of the first coding region or a 5' terminus of the second coding region," to exclude a signal sequence being located between the recited first and the second regions. Support for this amendment may be found at least at page 3, lines 9-13, page 6, line 22 and page 27, lines 8-9 of the specification and original claim 61.

In addition, claim 61 has been amended to recite "under conditions suitable for expression of the expression vector to produce the fused protein in a periplasm or a medium of said host cell," to even further clarify the claimed invention as suggested by the Examiner.

I. Preliminary Matters

Applicants thank the Examiner for returning signed and initialed copies of the PTO Forms SB/08 that accompanied the Information Disclosure Statements filed June 18, 2008 and July 23, 2008.

In the Office Action Summary, however, it appears that the Examiner inadvertently did not acknowledge i) receipt of the drawings filed on October 14, 2004, ii) Applicants' claim for foreign priority, or iii) receipt of the certified copy of the priority document filed on October 14, 2004. Applicants request that the Examiner acknowledge receipt of the drawings, Applicants' claim to priority, and receipt of the certified copy of the priority document in the next action.

II. Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 35 and 61 are rejected under 35 U.S.C. 112, second paragraph, as being allegedly indefinite. It appears that the Examiner inadvertently did not identify the statute under which these claims are rejected. Page 2, *Office Action of August 20, 2008*. However, as the previous Office Action of January 18, 2008 rejected claims 35 and 61 under 35 U.S.C. § 112, second paragraph, for reasons similar to those set forth in the present Office Action, Applicants assume that the rejection of claims 35 and 61 under 35 U.S.C. § 112, second paragraph, is maintained. Pages 3-5, *Office Action of January 18, 2008*. Applicants respectfully request the Office to clarify the specific statute under which claims 35 and 61 are rejected.

1. Claim 35 is asserted to be confusing in the recitation of "encoding a protease digestion site in the same reading frame as (a) and (b)" since (b) of the expression vector of claim 33 does not include a coding region but a restriction site into which a second coding region may be inserted. The Office Action suggests amending claim 35 to replace "in the same reading frame as (a) and (b)" with "in the same reading frame as (a)."

In response, Applicants have amended claim 35 to recite "in the same reading frame as (a)" as suggested by the Office Action.

2. Claim 61 is asserted to be unclear in the recitation of "a signal sequence at ... a 3' terminus of the second coding region" since signal sequences that provide for export into the periplasm or media when fused at the 3' terminus of a protein coding sequence are not known in the art. Moreover, the Examiner asserts that, even if claim 61 is amended to recite "5' terminus of the second coding region," the amended claim would still be confusing because the signal sequences that provide for export into the periplasm or media while being located within the interior of a protein, are not known, either.

The Examiner is thanked for pointing out that the Amendment filed on May 19, 2008 does not reflect the claim amendment to claim 61 as mentioned in the same amendment. In response, Applicants have amended claim 61 to recite "the 5' terminus of a coding region of the expression vector that encodes the N-terminus of the fused protein." Thus, amended claim 61 does not read on the signal sequence being located within the interior of a protein (i.e. between the recited first and the second regions).

Accordingly, withdrawal of the rejections under 35 U.S.C. §112, second paragraph is respectfully requested.

III. Claim Rejections Under 35 U.S.C. § 112, first paragraph, Written Description

Claim 61 is rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office Action asserts that the specification does not provide support for the recitation of "a signal sequence at ... a 3' terminus of the second coding region".

In response, Applicants note that claim 61 has been amended to correct a clerical error, and to replace "3' terminus" with "5' terminus." *See* page 6, line 22 and page 27, lines 8-9 of the specification. Accordingly, the above rejection is overcome.

Withdrawal of the written description rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

IV. Claim Rejections Under 35 U.S.C. § 112, first paragraph, Enablement

Claim 55 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated host cell transformed with the claimed expression vector, does not reasonably provide enablement for host cells within a multicellular organism that have been transformed with the recited expression vector. The Office Action suggests amending claim 55 to replace "[a] host" with "[a]n isolated host cell."

In response, and solely to advance prosecution of the present application, Applicants have amended claim 55 to recite "[a]n isolated host cell" as suggested by the Examiner.

Withdrawal of the enablement rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

V. Claim Rejections Under 35 U.S.C. § 103

Claims 33-37, 40-42, 53-56, and 59-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fersht (WO 00/75346; "Fersht") in view of Furutani *et al.* ("Furutani"), for reasons of record. Specifically, the Examiner asserts that Fersht indicates that any chaperone fragment can be used in the disclosed vector, and that, while Fersht does not teach a sequence encoding an archaebacterial FKBP-type PPIase, Furutani teaches a PPIase that has molecular chaperone activity. Thus the Examiner alleges that one of ordinary skill in the art would understand that the chaperone fragment of Fersht could be replaced with the PPIase disclosed by Furutani.

Applicants note that the present invention involves an expression vector comprising a coding region encoding an archaebacterial FKBP-type PPIase possessing an unexpectedly superior property in that it to produces a fused protein with hardly expressible proteins in a soluble form. Summary of Invention, page 4, lines 14-21, page 13, line 11-page 14, line 14, page 28, line 32-page 29, line 3, and Examples 1-3. The unexpectedly superior property is supported not only by the present specification but also by the 1.132 Declaration of Dr. Ideno filed on November 9, 2007. Namely, the presently claimed expression vector produces fused proteins with hardly expressible proteins, such as scFv antibody fragments, HCc, SerR, and the Endothelin A receptor, in a soluble form.

On the other hand, as shown in the 1.132 Declaration of Dr. Ideno filed on November 9, 2007, Fersht's expression vector fails to produce fused proteins with hardly expressible proteins, such as scFv antibody fragments, HCc, SerR, and the Endothelin A receptor, in either a soluble or insoluble fraction. Figure 2 and Results. Moreover, Furutani does not cure this deficiency because Furutani neither teaches nor suggests a fused protein or an expression vector to produce a fused protein using the FKBP (FK 506 binding protein).

With regard to the 1.132 Declaration of Dr. Ideno filed on November 9, 2007 and June 20, 2008, the Examiner maintains that the showing of the unexpectedly superior properties in the Declaration is not commensurate in scope with the scope of the presently claimed invention because there is no evidence in the art, the specification, and/or the Declaration showing that the unexpected results are due to the presence of an IF domain and/or C-terminal domain in the chaperone fragment.

In response, as suggested by the Examiner during an interview of February 13, 2009, Applicants submit (i) references teaching that the presence of an IF domain and/or C-terminal domain are critical in the activity of the archaebacterial FKBP-type PPIase (Furutani et al., Biochemistry, 39 (2), 453-462, 2000; Suzuki et al., J. Mol. Biol, 328, 1149-1160, 2003; Maruyama et al., Frontiers in Bioscience, 5, 821-836, 2000), (ii) a reference disclosing that other expression vectors comprising a coding region encoding the archaebacterial FKBP-type PPIases as recited in the present claims exhibit the same unexpected results (Ideno, et al., WO 2005/063964, filed on December 24, 2004), and (iii) a sequence alignment of the IF domain sequence and Fersht's GroE1 sequence showing that the IF domain is not present in GroE1.

Specifically, the Furutani's Biochemistry reference discloses MTFKs (FKBPs; FK506 binding proteins) with and without the IF domain and teaches that an IF domain, called a flap insertion, is required for chaperone activity in MTFKs. Abstract, page 460, lines 31-35 of right column. The Suzuki reference teaches the structure of the IF domain and discloses that the IF domain exposes a hydrophobic surface, which may play an important role in the chaperone-like activity, which suggests a relationship between the structure and the function of the IF domain. Abstract. Moreover, the Maruyama reference teaches that both short-type and long-type archaebacterial FKBP-type PPIase include the IF domain. Figure 3 and page 826, line 24 of left column to line 11 of right column.

Moreover, as shown in WO 2005/063964 and its translation, other expression vectors comprising a coding region encoding the archaebacterial FKBP-type PPIases, such as pMal7F2 and pMm18F2, produce fusion proteins with hardly expressible proteins in a soluble form. Examples 3-4 and 10-16.

Based on the evidence presented above, one of ordinary skill in the art would understand that the IF domain and/or C-terminus is critical to the activity of the archaebacterial FKBP-type PPIases and that TcFKfusion2, pMal7F2 and pMm18F2 comprising a coding region encoding the archaebacterial FKBP-type PPIases are representative of the claimed expression vector. One of ordinary skill in the art would confirm such understanding by the evidence that the IF domain is a feature of the archaebacterial FKBP-type PPIases, but not of Fersht's GroE1.

Thus, Applicants assert that the showing of the unexpectedly superior properties in the Declaration of Dr. Ideno filed on November 9, 2007 is commensurate in scope with the scope of

the presently claimed invention and is sufficient to overcome the above obviousness rejection under 35 U.S.C. 103(a).

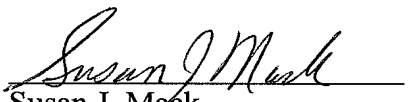
Withdrawal of the obviousness rejection under 35 U.S.C. §103 is respectfully requested.

VI. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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